

=> s (interleukin 1-beta) or IL-1.beta.

L1 27718 (INTERLEUKIN 1-BETA) OR IL-1.BETA.

=> s l1 (20a) intravitr#####

L2 22 L1 (20A) INTRAVITR#####

=> s l2 (40a) (retinal or macular?)

L3 5 L2 (40A) (RETINAL OR MACULAR?)

=> duplicate remove

ENTER L# LIST OR (END):l2

DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS, USPATFULL'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L2
L4 15 DUPLICATE REMOVE L2 (7 DUPLICATES REMOVED)

=> duplicate remove

ENTER L# LIST OR (END):l3

DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS, USPATFULL'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L3
L5 3 DUPLICATE REMOVE L3 (2 DUPLICATES REMOVED)

=> d 1-3

L5 ANSWER 1 OF 3 USPATFULL
AN 2000:109333 USPATFULL
TI Replication competent, avirulent Herpes simplex virus as a vector for
neural and ocular gene therapy
IN Brandt, Curtis R., Oregon, WI, United States
Kalil, Ronald E., Madison, WI, United States
Agarwala, Seema, Evanston, IL, United States
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S.
corporation)
PI US 6106826 20000822
AI US 1997-992250 19971217 (8)
DT Utility
LN.CNT 903
INCL INCLM: 424/093.200
INCLS: 514/044.000; 435/320.100; 435/235.100
NCL NCLM: 424/093.200
NCLS: 514/044.000; 435/320.100; 435/235.100
IC [7]
ICM: A01N063-00
ICS: A01N043-04; C12N015-63
EXF 435/320.1; 435/235.1; 435/325; 435/455; 424/93.2; 514/44; 536/23.5;
536/24.1

L5 ANSWER 2 OF 3 MEDLINE
 AN 97159007 MEDLINE
 DN 97159007
 TI Interleukin-1 beta-induced disruption of the retinal vascular barrier of the central nervous system is mediated through leukocyte recruitment and histamine.
 AU Bamforth S D; Lightman S L; Greenwood J
 CS Department of Clinical Ophthalmology, University College London, United Kingdom.
 SO AMERICAN JOURNAL OF PATHOLOGY, (1997 Jan) 150 (1) 329-40.
 Journal code: 3RS. ISSN: 0002-9440.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
 EM 199704
 EW 19970403

DUPLICATE 2

L5 ANSWER 3 OF 3 MEDLINE
 AN 95095545 MEDLINE
 DN 95095545
 TI Interleukin-1-beta changes the expression of metalloproteinases in the vitreous humor and induces membrane formation in eyes containing preexisting retinal holes.
 AU Kosnosky W; Li T H; Pakalnis V A; Fox A; Hunt R C
 CS Department of Ophthalmology, University of South Carolina School of Medicine, Columbia 29208.
 NC EY06164 (NEI)
 EY10516 (NEI)
 SO INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1994 Dec) 35 (13) 4260-7.
 Journal code: GWI. ISSN: 0146-0404.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199503

=> d 1-3 hit

L5 ANSWER 1 OF 3 USPATFULL
 SUMM As briefly discussed above, various polypeptides are useful for treatment of ocular and neural diseases. For example, subretinal or **intravitreal** injection of a number of growth factors, cytokines and neurotrophins (bFGF, brain derived growth factor, **interleukin-1.beta.**) have been shown to restore specific functions to **retinal** or **retinal** pigment epithelial cells and to retard photoreceptor cell death in various animal models of **retinal** degeneration. Faktorovich et al., Nature 347:83 (1990); LaVail et al., Proc. Nat'l Acad. Sci. USA 89:11249 (1992). Moreover, Faktorovich et al., Nature 347:83 (1990), have shown that the rate of photoreceptor degeneration can be significantly slowed by an intraocular injection of bFGF in Royal College of Surgeons rats that have inherited retinal dystrophy. Intraocular administration of bFGF also protects photoreceptors from light-induced degeneration in albino rats, a noninherited form of retinal degeneration. LaVail et al., Ann. N.Y. Acad. Sci. 638:341 (1991).

L5 ANSWER 2 OF 3 MEDLINE
 AB The vascular barriers of the central nervous system form a selective cellular interface between the blood and the neural parenchyma and

DUPLICATE 1

restrict the transfer of both molecules and hematogenous cells. During immune-mediated diseases, leukocyte infiltration becomes dramatically up-regulated and the permeability of these barriers increases, leading to edema formation. The etiology of this damage remains largely unresolved although inflammatory cytokines have been implicated in the process. The effect of the proinflammatory cytokine interleukin (IL)-1 beta on the integrity of the rat blood-retinal barrier (BRB) was investigated up to 14 days after an intravitreal injection. The permeability of the BRB was evaluated quantitatively using the low molecular weight tracer [14C]mannitol. After IL-1 beta administration, a biphasic opening of the BRB to [14C]mannitol was recorded, peaking at 4 to 8 hours and 24 to 48 hours post-injection (PI). The early disruption coincided with the appearance

of both polymorphonuclear and mononuclear leukocytes within the retina. By 12

hours PI, BRB permeability had returned to control values despite a continued increase in the number of infiltrating leukocytes. The second, more pronounced increase in barrier permeability detected at 24 to 48 hours PI corresponded with maximal leukocyte infiltration. Barrier dysfunction had resolved by 72 hours, and by 7 days the leukocyte infiltrate had disappeared. The IL-1 beta-induced increase in

permeability

could be completely abrogated at 4 and 24 hours PI by treating the

animals

with the histamine H2-receptor antagonist ranitidine, which also reduced leukocyte infiltration by 47.2%. The ability of histamine to disrupt the BRB was demonstrated by intravitreal and intravascular administration, which caused a rapid and significant increase in BRB permeability. Treatment of the animals with the cyclo-oxygenase inhibitor indomethacin had no effect on IL-1 beta-induced disruption of the BRB at 4 hours PI, but by 24 hours PI a significant reduction in permeability was observed that coincided with a 75.2% reduction in the leukocyte infiltrate. The depletion of circulating leukocytes to < 2% of control levels reduced the retinal leukocyte recruitment induced by IL-1 beta by 73.0% and decreased BRB permeability at both 4 and 24 hours after IL-1 beta injection. These data demonstrate that intravitreal IL-1 beta in the rat induces a biphasic opening of the BRB that appears to be mediated through recruited leukocytes and release of the vasoactive amine histamine.

L5 ANSWER 3 OF 3 MEDLINE

DUPLICATE 2

AB PURPOSE. Proliferative vitreoretinopathy occurs when cells migrate into the vitreous humor, where they proliferate and produce a membrane composed

of extracellular matrix. Interleukin-1-beta (IL-1-beta) may be involved in

these processes because it is chemotactic and mitogenic, and it stimulates

metalloproteinase production. In the present study, the effects of intravitreally injected IL-1-beta on retinal membrane formation and the associated changes in metalloproteinase content of vitreous humor were examined. METHODS.

Rabbit

eyes were injected with IL-1-beta in a buffer, with or without the prior creation of retinal holes. Control eyes received the buffer alone or no injection, with or without retinal holes. Animals were examined by slit lamp biomicroscopy and indirect ophthalmoscopy for 1 month. Zymography was performed on a portion of vitreous humor to assess collagenase content, and the remaining tissue was subjected to histologic analysis. RESULTS. Intraocular IL-1-beta induced perilimbal vessel engorgement, keratic precipitates, synechiae, flare, lens deposits, optic disk hyperemia, and granulomatous formations that gradually subsided during the first week. Intravitreal injection of IL-1-beta in eyes with preexisting retinal holes

additionally induced membrane formation. Zymographic analysis of vitreous humor from animals sacrificed 24 hours after IL-1-beta injection showed a 100-kd and a 65-kd gelatinase, whereas control vitreous humor contained predominantly a single gelatinase species of approximately 65 kd. Retinal holes did not affect IL-1-beta induction of the 100-kd gelatinase.

CONCLUSIONS. IL-1-beta induces a 100-kd gelatinase in the vitreous humor and epiretinal membrane formation in eyes containing preexisting retinal holes. The presence of retinal holes and abnormal production of cytokines may lead to a cascade of events, including aberrant extracellular matrix remodeling, that result in proliferative diseases of the eye.

=> d hist

(FILE 'HOME' ENTERED AT 11:38:09 ON 11 SEP 2000)

FILE 'MEDLINE, BIOSIS, USPATFULL, PCTFULL' ENTERED AT 11:38:29 ON 11 SEP 2000

L1 27718 S (INTERLEUKIN 1-BETA) OR IL-1.BETA.
 L2 22 S L1 (20A) INTRAVITR####
 L3 5 S L2 (40A) (RETINAL OR MACULAR?)
 L4 15 DUPLICATE REMOVE L2 (7 DUPLICATES REMOVED)
 L5 3 DUPLICATE REMOVE L3 (2 DUPLICATES REMOVED)

=> d 14 1-15

L4 ANSWER 1 OF 15 USPATFULL
 AN 2000:109333 USPATFULL
 TI Replication competent, avirulent Herpes simplex virus as a vector for neural and ocular gene therapy
 IN Brandt, Curtis R., Oregon, WI, United States
 Kalil, Ronald E., Madison, WI, United States
 Agarwala, Seema, Evanston, IL, United States
 PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
 PI US 6106826 20000822
 AI US 1997-992250 19971217 (8)
 DT Utility
 LN.CNT 903
 INCL INCLM: 424/093.200
 INCLS: 514/044.000; 435/320.100; 435/235.100
 NCL NCLM: 424/093.200
 NCLS: 514/044.000; 435/320.100; 435/235.100
 IC [7]
 ICM: A01N063-00
 ICS: A01N043-04; C12N015-63
 EXF 435/320.1; 435/235.1; 435/325; 435/455; 424/93.2; 514/44; 536/23.5; 536/24.1

L4 ANSWER 2 OF 15 MEDLINE
 AN 1998295148 MEDLINE
 DN 98295148
 TI Involvement of TNF alpha, IL-1 beta and IL-1 receptor antagonist in LPS-induced rabbit uveitis.
 AU Mo J S; Matsukawa A; Ohkawara S; Yoshinaga M
 CS Department of Pathology, Kumamoto University School of Medicine, Japan.
 SO EXPERIMENTAL EYE RESEARCH, (1998 May) 66 (5) 547-57.
 Journal code: EPL. ISSN: 0014-4835.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199810

EW 19981001

DUPLICATE 1

L4 ANSWER 3 OF 15 MEDLINE
AN 97159007 MEDLINE
DN 97159007
TI Interleukin-1 beta-induced disruption of the retinal vascular barrier of the central nervous system is mediated through leukocyte recruitment and histamine.
AU Bamforth S D; Lightman S L; Greenwood J
CS Department of Clinical Ophthalmology, University College London, United Kingdom.
SO AMERICAN JOURNAL OF PATHOLOGY, (1997 Jan) 150 (1) 329-40.
Journal code: 3RS. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199704
EW 19970403

L4 ANSWER 4 OF 15 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:407982 BIOSIS
DN PREV199799714185
TI Blood-retinal barrier (BRB) breakdown in experimental autoimmune uveoretinitis: Comparison with vascular endothelial growth factor, tumor necrosis factor alpha, and interleukin-1-beta-mediated breakdown.
AU Luna, Jose D.; Chan, Chi-Chao; Derevjani, Nancy L.; Mahlow, Jeremy; Chiu, Charlie; Peng, Bo; Tobe, Takao; Campochiaro, Peter A.; Vinore, Stanley
A.
(1)
CS (1) 825 Maumenee, Johns Hopkins Univ. Sch. Med., 600 N. Wolfe St., Baltimore, MD 21287-9289 USA
SO Journal of Neuroscience Research, (1997) Vol. 49, No. 3, pp. 268-280.
ISSN: 0360-4012.
DT Article
LA English

DUPLICATE 2

L4 ANSWER 5 OF 15 MEDLINE
AN 97117495 MEDLINE
DN 97117495
TI Interleukin 1 in experimental proliferative vitreoretinopathy.
AU Osusky R; Tao L; Ryan S J
CS Department of Ophthalmology, School of Medicine, University of Southern California, Los Angeles, USA.
NC EYO-3040
EYO-1545
SO OPHTHALMOLOGICA, (1997) 211 (1) 49-52.
Journal code: OIG. ISSN: 0030-3755.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
EW 19970503

DUPLICATE 3

L4 ANSWER 6 OF 15 MEDLINE
AN 97161370 MEDLINE
DN 97161370
TI Ultrastructural analysis of interleukin-1 beta-induced leukocyte recruitment to the rat retina.
AU Bamforth S D; Lightman S L; Greenwood J
CS Division of Clinical Science, University College London, United Kingdom.
SO INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1997 Jan) 38 (1) 25-35.

Journal code: GWI. ISSN: 0146-0404.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
EW 19970403

L4 ANSWER 7 OF 15 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:73027 BIOSIS
DN PREV199799372230
TI Vitreous changes during ocular inflammation induced by interleukin 1-beta.

AU Hikichi, Taiichi (1); Ueno, Norio; Chakrabarti, B.; Trempe, C. L.; Yoshida, Akitoshi
CS (1) Dep. Ophthalmology, Asahikawa Med. Coll., 4-5 Nishikagura, Asahikawa-shi, Hokkaido 078 Japan
SO Nippon Ganka Gakkai Zasshi, (1996) Vol. 100, No. 11, pp. 853-857. ISSN: 0029-0203.
DT Article
LA Japanese
SL Japanese; English

L4 ANSWER 8 OF 15 MEDLINE
AN 97142192 MEDLINE
DN 97142192
TI Vitreous changes during ocular inflammation induced by interleukin 1 beta.

AU Hikichi T; Ueno N; Chakrabarti B; Trempe C L
CS Schepens Eye Research Institute, Department of Ophthalmology, Harvard Medical School, Boston, USA.
SO JAPANESE JOURNAL OF OPHTHALMOLOGY, (1996) 40 (3) 297-302. Journal code: KN1. ISSN: 0021-5155.

CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
EW 19970602

L4 ANSWER 9 OF 15 MEDLINE
AN 95300936 MEDLINE
DN 95300936
TI Inflammation induced changes in adenosine 3',5'-cyclic monophosphate production by ciliary epithelial cell bilayers.
AU Fleisher L N; Ferrell J B; McGahan M C
CS North Carolina State University, College of Veterinary Medicine, Department of Anatomy, Physiological Sciences and Radiology, Raleigh 27606, USA..
NC EY08688 (NEI)
SO EXPERIMENTAL EYE RESEARCH, (1995 Feb) 60 (2) 165-71. Journal code: EPL. ISSN: 0014-4835.

CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199509

L4 ANSWER 10 OF 15 MEDLINE
AN 95247056 MEDLINE
DN 95247056
TI Mediators of the ocular inflammatory response to interleukin-1 beta plus tumor necrosis factor-alpha.
AU Fleisher L; Ferrell J; McGahan C
CS North Carolina State University, College of Veterinary Medicine, Raleigh

DUPLICATE 4

27606, USA..
NC EY-08688 (NEI)
SO GRAEFES ARCHIVE FOR CLINICAL AND EXPERIMENTAL OPHTHALMOLOGY, (1995 Feb)
233 (2) 94-100.
Journal code: FPR. ISSN: 0721-832X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199508

L4 ANSWER 11 OF 15 MEDLINE DUPLICATE 5
AN 95319664 MEDLINE
DN 95319664
TI Tolerance of **intravitreal** **interleukin-1**
beta in the treatment of experimental vitreous hemorrhage.
AU Pastor J C; Gonzalez O; Saavedra J A; Guerra A; Angulo S
CS Instituto de Oftalmobiologia Aplicada, Valladolid Medical School,
University of Valladolid, Spain..
SO OPHTHALMIC RESEARCH, (1995) 27 (1) 37-41.
Journal code: OIE. ISSN: 0030-3747.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199510

L4 ANSWER 12 OF 15 MEDLINE DUPLICATE 6
AN 95095545 MEDLINE
DN 95095545
TI Interleukin-1-beta changes the expression of metalloproteinases in the
vitreous humor and induces membrane formation in eyes containing
preexisting retinal holes.
AU Kosnosky W; Li T H; Pakalnis V A; Fox A; Hunt R C
CS Department of Ophthalmology, University of South Carolina School of
Medicine, Columbia 29208.
NC EY06164 (NEI)
EY10516 (NEI)
SO INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1994 Dec) 35 (13)
4260-7.
Journal code: GWI. ISSN: 0146-0404.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503

L4 ANSWER 13 OF 15 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:200088 BIOSIS
DN PREV199497213088
TI Efficacy and ocular and systemic tolerance of **intravitreal**
injection of **interleukin-1 beta** (IL
-1-beta) in experimental vitreous hemorrhages.
AU Pastor, J. C. (1); Guerra, A. (1); Gonzalez, O. (1); Saavedra, J. A. (1);
Angulo, S. (1); Gonzalez, E.; Saornil, M. A. (1)
CS (1) Vitreo Unit, Instituto de Oftalmobiologia Aplicada, Univ. Valladolid,
Valladolid Spain
SO Investigative Ophthalmology & Visual Science, (1994) Vol. 35, No. 4, pp.
1534.
Meeting Info.: Annual Meeting of the Association for Research in Vision
and Ophthalmology Sarasota, Florida, USA May 1-6, 1994
ISSN: 0146-0404.
DT Conference
LA English

AN 93231259 MEDLINE
DN 93231259
TI Studies on intraocular inflammation produced by intravitreal human interleukins in rabbits.
AU Kulkarni P S; Mancino M
CS Department of Ophthalmology and Visual Sciences, Kentucky Lions Eye Research Institute, University of Louisville, School of Medicine 40292..
NC EY 02861.(NEI)
SO EXPERIMENTAL EYE RESEARCH, (1993 Mar) 56 (3) 275-9.
Journal code: EPL. ISSN: 0014-4835.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199307

L4 ANSWER 15 OF 15 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1991:243757 BIOSIS
DN BR40:117922
TI INFLAMMATORY RESPONSE TO **INTRAVITREALLY-INJECTED TUMOR NECROSIS FACTOR-ALPHA TNFALPHA AND INTERLEUKIN-1-BETA IL-1-BETA.**
AU FLEISHER L N; FERRELL J B; MCGAHAN M C
CS COLL. VET. MED., N.C. STATE UNIV., RALEIGH, N.C. 27606.
SO ANNUAL SPRING MEETING OF THE ASSOCIATION FOR RESEARCH IN VISION AND OPHTHALMOLOGY, SARASOTA, FLORIDA, USA, APRIL 28-MAY 3, 1991. INVEST OPHTHALMOL VISUAL SCI. (1991) 32 (4), 677.
CODEN: IOVSDA. ISSN: 0146-0404.
DT Conference
FS BR; OLD

(FILE 'HOME' ENTERED AT 10:51:31 ON 11 SEP 2000)

FILE 'MEDLINE, BIOSIS, USPATFULL, PCTFULL' ENTERED AT 10:51:46 ON 11 SEP 2000

L1 84179 S (INTERLEUKIN 1-BETA) OR IL-1#
L2 855 S L1 (40A) (RETIN#### OR OPTIC## OR MACULAR)
L3 690 DUPLICATE REMOVE L2 (165 DUPLICATES REMOVED)
L4 369 S L3 (40A) (ADMINIST##### OR INJECT### OR TREAT####)
L5 726 S L1 (20A) (RETIN#### OR OPTIC## OR MACULAR)
L6 357 S L5 (20A) (ADMINIST##### OR INJECT### OR TREAT####)
L7 322 DUPLICATE REMOVE L6 (35 DUPLICATES REMOVED)
L8 55 S L7 (20A) NEURON##
L9 5 S L8 (20A) (NEURON## (4A) SURVIV##)